Machine translation JP11322948

(19) **Publication country** Japan Patent Office (JP)
(12) **Kind of official gazette** Open patent official report (A)
(11) **Publication No.** JP,11-322948,A
(43) **Date of Publication** November 26, Heisei 11 (1999)
(54) **Title of the Invention** A macromolecule particle and its manufacture approach
(51) **International Patent Classification (6th Edition)**

C08J 3/12
// C08L101/00

FI

C08J 3/12 Z
C08L101/00

Request for Examination Un-asking.
The number of claims 3
Mode of Application OL
Number of Pages 7
(21) **Application number** Japanese Patent Application No. 10-126084
(22) **Filing date** May 8, Heisei 10 (1998)
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(57) **Abstract**
Technical problem The macromolecule particle which has biodegradability useful as a drug carrier and biocompatibility, and its manufacture approach are offered.
Means for Solution The following general formula (1)
Formula 1

(However, among a formula, R1, R2, and R3 show a hydrogen atom or the alkyl group of carbon numbers 1-4, you may be a radical which is different even when it is the same, and n shows the integer of 1-4.) Carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed. The particle to which it is the macromolecule particle which consists of a becoming polymer (A) and a biodegradable polymer (B), and a polymer (A) comes to exist on the surface of a biodegradable polymer (B).

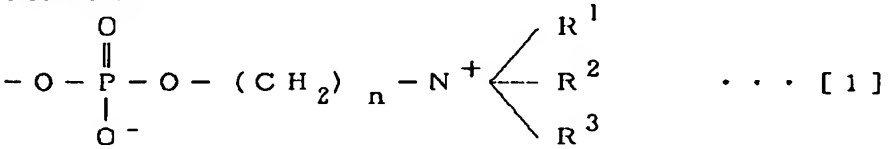
Claim(s)
Claim 1 The following general formula (1)

Formula 1

(However, R1, R2, and R3 show a hydrogen atom or the alkyl group of carbon numbers 1-4 among a formula.) even if the same, you may be a different radical, and n shows the integer of 1-4. The macromolecule particle to which it is the macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed, and a biodegradable polymer (B), and a polymer (A) comes to exist on the surface of a biodegradable polymer (B).

Claim 2 The following general formula (1)

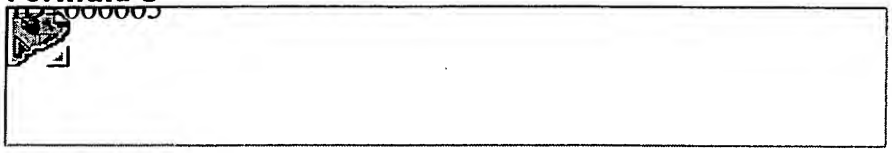
Formula 2



(-- however, among a formula, R1, R2, and R3 show a hydrogen atom or the alkyl group of carbon numbers 1-4, you may be a radical which is different even when it is the same, and n shows the integer of 2.) -- macromolecule particle to which it is the macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed and a polyhydroxy acid, and a polymer (A) comes to exist in the front face of a polyhydroxy acid.

Claim 3 The following general formula (1)

Formula 3



(However, R1, R2, and R3 show a hydrogen atom or the alkyl group of carbon numbers 1-4 among a formula.) even if the same, you may be a different radical, and n shows the integer of 1-4. It is the manufacture approach of a macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed, and a biodegradable polymer (B). The manufacture approach of the macromolecule particle according to claim 1 characterized by distributing a biodegradable polymer (B) in the water solution of said polymer (A).

Example Hereafter, an example explains to a detail. In addition, the analysis apparatus and measuring method which were used are as follows.

1. Measurement of the MPC content in a polymer (mol %); measurement of 1 H-MNR to the MPC origin - N(CH3) 3 and butyl of n-butyl methacrylate - It computed from CH3.
2. measurement **of F-potential** ; -- measurement of the F-potential of a particle -- a model; F-potential measurement machine and the product made from the Otsuka electron -- ELS-800 and a migration solvent were performed using the phosphoric-acid physiological saline.
3. The measurement 1; atomic force microscope model of particle size of the measurement; particle which is the particle size of a particle; product made from SEIKO electronic industry, scan mold probe microscope, system SPI-3800.

Conditions; after distributing cantilever SI-DF20 use and an approach; particle on a glass plate, it observed in DFM mode.

The measurement 2; electron microscope model of particle size of a particle; it observed, after dyeing and carrying out carbon shadowing of the JEOL make, JSM-5400, and the condition; particle with an osmic acid.

4. The density measurement; model which is a particle; concentration was measured and computed from vibration frequency using the Xtal dispatch child (Hokuto Denko make).
5. Measurement of Alpha-helix Content in Cow Serum Albumin;

Model; the Jasco make, JASCO J-720W conditions; it measured by the circular dichroism (CD) spectrum in 222nm.

0028 Into synthetic example 1 ethanol, one mol /of azobisisobutyronitrils was further adjusted to the concentration of 5 millimols / liter as a polymerization initiator I., and the polymerization of the monomer constituent (30/70; mol %) of 2-(methacryloyloxy) ethyl-2-(trimethylammonio) ethyl phosphate (Following MPC and brief sketch) and n-butyl methacrylate (Following BMA and brief sketch) was carried out at 60 degrees C for 2 hours. After having dropped the reaction mixture at the ether after reaction termination, carrying out the precipitating copolymer the ** exception and removing a residual monomer, reduced pressure drying was carried out and the MPC-BMA copolymer (it outlines Following PMB) was obtained. The analysis result of obtained PMB was shown below.

yield: -- MPC content **in a 70 % of the weight copolymer** : -- 30 mol %IR(cm-1):2800-3000, 1730 and 1400, and 1200 molecular weight: MW=68,000 **0029** PMB compounded by the example 1 of example 1 composition was dissolved in distilled water, and it adjusted to the concentration of 1 mg/mL. Next, 20mg (PLA-0020, the Wako Pure Chem make, weight average molecular weight = 20,000) of Polly L-lactic acid was dissolved in methylene chloride 2mL. It dropped one drop of methylene chloride solution of the above-mentioned polylactic acid at a time, having soaked the PMB water solution into the ice bath, and stirring by 400rpm. Sonication equipment (product made from BRANSON SONIC POWER COMPAN) performed processing for 30 minutes after dropping termination. After distilling off a methylene chloride under reduced pressure, the particle was made to sediment according to centrifugal separation (for **10300** G or 30 minutes). After having removed the supernatant, adding distilled water 40 mLs and re-distributing a particle, the particle was made to sediment according to centrifugal separation (for **10300** G or 30 minutes). The same actuation was repeated a total of 3 times, and the macromolecule particle was obtained. The obtained macromolecule particle was distributed, vibration frequency was measured using the Xtal dispatch child (Hokuto Denko make), and the concentration of a particle was computed. Moreover, the particle size of the obtained particle was measured using the atomic force microscope and the electron microscope. Furthermore, F-potential measurement of a particle was performed.

yield **of a macromolecule particle** : -- particle-size **of 10% macromolecule particle** : -- about 100nm F-potential: -- as a result of the -10mV above-mentioned measurement, the particle was spherical and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.

0030 Except having changed into 0.5 mg/mL the PMB water-solution concentration used in the example 2 example 1, the same actuation as an example 1 was performed, and the target macromolecule particle was obtained.

yield **of a macromolecule particle** ; -- particle-size **of 10% macromolecule particle** ; -- about 160nm F-potential: -- the particle was spherical as well as the -10mV example 1, and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.

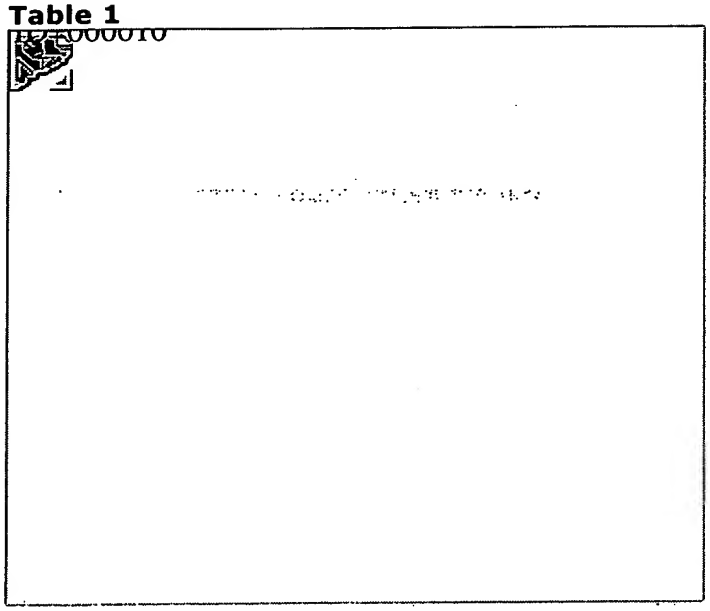
0031 Except having changed into 0.1 mg/mL the PMB water-solution concentration used in the example 3 example 1, the same actuation as an example 1 was performed, and the target macromolecule particle was obtained.

yield **of a macromolecule particle** ; -- particle-size **of 10% macromolecule particle** ; -- about 170nm F-potential: -- the particle was spherical as well as the -10mV example 1, and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.

0032 The giant-molecule particle adjusted to the phosphoric-acid buffer water solution (concentration 0.1 mg/mL) of example of reference 1 cow serum albumin in the example 1 was added, and it incubated at 37 degrees C for 3 hours. The circular dichroism spectrum of cow serum albumin was measured after processing, and the content of the alpha helix in cow serum albumin was calculated. The result was shown in Table 1.

0033

Table 1



0034 From the above result, not being influenced by the concentration of a macromolecule particle becomes clear and it can be said that it has biocompatibility.

DETAILED DESCRIPTION

Detailed Description of the Invention

0001

Field of the Invention This invention relates to a macromolecule particle and its manufacture approach. It is related with the macromolecule particle which has the outstanding biocompatibility and safety in detail, and its manufacture approach. It is related with a macromolecule particle useful as a drug carrier, and its manufacture approach in more detail.

0002

Description of the Prior Art The concept of a drug delivery system (DDS) of medicating with the drugs of a complement the location required by the way which is the need is considered to be a very effective means from a viewpoint of the effectiveness of a therapy, improvement in safety, and derating to a patient. A water soluble polymer, liposome, the macromolecule particle, the macromolecule micell, etc. are used for the drug carrier used for this DDS (Society of Synthetic Organic Chemistry, Japan, the 55th volume, No. 5, 430 pages, 1997). However, the common technical problem of these drug carriers is a point of whether a drug is made to reach the organ which avoids the incorporation by the reticuloendothelial system which is a living body's foreign matter incorporation device how, and serves as a target, and a cell. In order to solve this technical problem, the attempt which makes the front face of a drug carrier embellish a hydrophilic macromolecule is made. For example, liposome which embellished the polyethylene glycol (FEBES Letter, the 284th volume, 263 pages, 1991), The macromolecule micell (Critical Reviews in Therapeutic Drug Carrier Systems, the 9th volume, 213 pages, 1992) which consists of a block copolymer of a polyethylene glycol and an aspartic acid, the macromolecule particle (FEBES Letter, the 167th volume, 79 pages, 1984) to which the copolymer of a polyethylene glycol and a polypropylene glycol was made to stick are known. As for the drug carrier of these hydrophilic-properties macromolecule qualification, the retentivity in the inside of blood is improved as compared with non-embellished it. However, since biocompatibility is still inadequate, there are many rates incorporated by the reticuloendothelial system and the further improvement is called for. On the other hand, when a drug is carried and the duty is completed, as for a drug carrier, being promptly discharged by the outside of the body is desirable. Generally, since molecular weight becomes the cause by which the trap of the 50,000 or more macromolecules is carried out by the filtration from mesangium, and are recording toxicity is generated, there is not little what is accumulated also into the drug carrier of said instantiation in the living body.

Therefore, the incorporation by the reticuloendothelial system is avoided, the macromolecule particle excellent in safety is called for, and the present condition is that the macromolecule particle which was still excellent in biocompatibility and safety is not reported.

0003

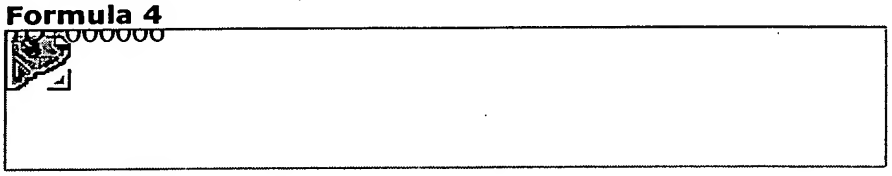
Problem(s) to be Solved by the Invention The purpose of this invention is to offer the macromolecule particle excellent in biocompatibility and safety, and its manufacture approach.

0004

Means for Solving the Problem As a result of inquiring in view of said trouble, artificers found out the macromolecule particle by the combination of a specific polymer and a biodegradable polymer, and completed this invention. According to this invention, it is the following general formula (1).

0005

Formula 4

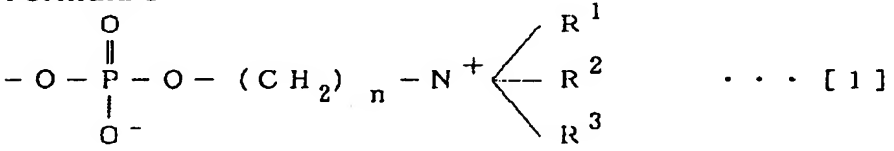


0006 (However, R1, R2, and R3 show a hydrogen atom or the alkyl group of carbon numbers 1-4 among a formula.) even if the same, you may be a different radical, and n shows the integer of 1-4. The macromolecule particle in which are the macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed, and a biodegradable polymer (B), and a polymer (A) comes to exist on the surface of a biodegradable polymer (B) is offered.

0007 Moreover, according to this invention, it is the following general formula (1).

0008

Formula 5



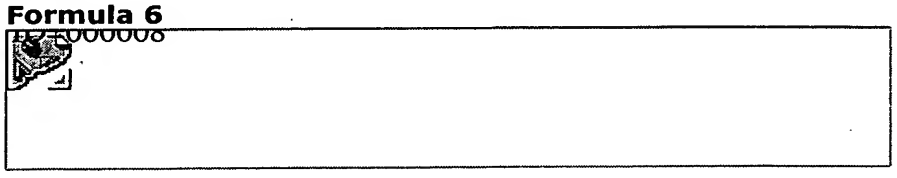
$$-O-\overset{\overset{O}{\|}}{\underset{\underset{O^-}{|}}{P}}-O-(CH_2)_n-N^+\begin{cases}R^1\\R^2\\R^3\end{cases} \quad \cdots [1]$$

0009 (However, R1, R2, and R3 show the alkyl group of a hydrogen atom or the carbon atomic numbers 1-4 among a formula.) even if the same, you may be a different radical, and n shows the integer of 2. The macromolecule particle to which are the macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed, and a polyhydroxy acid, and a polymer (A) comes to exist in the front face of a polyhydroxy acid is offered.

0010 According to this invention furthermore, it is the following general formula (1).

0011

Formula 6



0012 (However, R1, R2, and R3 show the alkyl group of a hydrogen atom or the carbon atomic numbers 1-4 among a formula.) even if the same, you may be a different radical, and n shows the integer of 1-4. It is the manufacture approach of a macromolecule particle which consists of a polymer (A) which comes to carry out the polymerization of the monomer constituent containing the monomer which has the side chain with which it is expressed, and a biodegradable polymer (B). The manufacture approach of the aforementioned particle characterized by distributing said polymer (A) and manufacturing a biodegradable polymer (B) is offered.

0013

Embodiment of the Invention The macromolecule particle of this invention is a particle which consists of said polymer (A) and said biodegradable polymer (B), and means the particle to which said polymer (A) comes to exist in the front face of said biodegradable polymer (B). The semantics of "the particle which comes to exist in a front face" is meant also including the particle which forms the form out of which the particle which said polymer (A) comes to cover on the front face of said biodegradable polymer (B), and said some of polymers (A) mingled with said

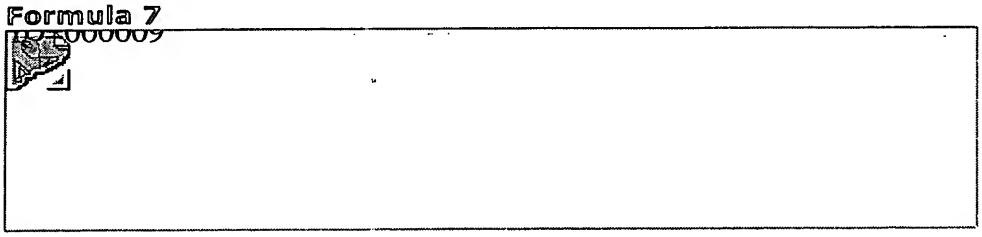
biodegradable polymer (B), and said some of polymers (A) have come to the outer layer of a particle. As for the configuration of the macromolecule particle of this invention, it is desirable that it is a globular form, the particle size has 1nm - desirable 100,000nm, and 10nm - its 1,000nm is more desirable.

0014 The monomer which has the radical expressed with the aforementioned general formula 1 used for the macromolecule particle of this invention in a side chain should just have the radical specifically expressed with the double bond of polymerization nature, and the aforementioned general formula 1 in a molecule. As this monomer, specifically For example, 2-(meta) acryloyloxyethyl-2'-(trimethylammonio) ethyl phosphate, 3-(meta) acryloyloxypropyl-2'-(trimethylammonio) ethyl phosphate, 4-(meth)acryloyloxy butyl-2'-(trimethylammonio) ethyl phosphate, 5-(meth)acryloyloxy pentyl-2'-(trimethylammonio) ethyl phosphate, 2-(meta) acryloyloxyethyl-2'-(triethyl ammonio) ethyl phosphate, 3-(meta) acryloyloxypropyl-2'-(triethyl ammonio) ethyl phosphate, 4-(meth)acryloyloxy butyl-2'-(triethyl ammonio) ethyl phosphate, 5-(meth)acryloyloxy pentyl-2'-(triethyl ammonio) ethyl phosphate, 2-(meta) acryloyloxyethyl-2'-(TORIPURO pill ammonio) ethyl phosphate, 3-(meta) acryloyloxypropyl-2'-(TORIPURO pill ammonio) ethyl phosphate, 4-(meth)acryloyloxy butyl-2'-(TORIPURO pill ammonio) ethyl phosphate, 5-(meth)acryloyloxy pentyl-2'-(TORIPURO pill ammonio) ethyl phosphate, 2-(meta) acryloyloxyethyl-2'-(tributyl ammonio) ethyl phosphate, 3-(meta) acryloyloxypropyl-2'-(tributyl ammonio) ethyl phosphate, 4-(meth)acryloyloxy butyl-2'-(TORIPURO pill ammonio) ethyl phosphate, 5-(meth)acryloyloxy pentyl-2'-(tributyl ammonio) ethyl phosphate, 2-(meta) acryloyloxyethyl-3'-(trimethylammonio) propyl phosphate, 2-(meta) acryloyloxyethyl-4'-(trimethylammonio) butyl ethyl phosphate, 2-(meta) acryloyloxyethyl-3'-(triethyl ammonio) propyl phosphate, 2-(meta) acryloyloxyethyl-4'-(triethyl ammonio) butyl phosphate, 2-(meta) acryloyloxyethyl-3 '- (TORIPURO pill ammonio) propyl phosphate and 2-(meta) acryloyloxyethyl -4'-(TORIPURO pill ammonio) butyl phosphate, 0015 Furthermore, 2-(meta) acryloyloxyethyl-3'-(tributyl ammonio) propyl phosphate, 2-(meta) acryloyloxyethyl-4'-(tributyl ammonio) butyl phosphate, 3-(meta) acryloyloxypropyl-3'-(trimethylammonio) propyl phosphate, 3-(meta) acryloyloxypropyl-4'-(trimethylammonio) butyl phosphate, 3-(meta) acryloyloxypropyl-3'-(triethyl ammonio) propyl phosphate, 3-(meta) acryloyloxypropyl-4'-(triethyl ammonio) butyl phosphate, 3-(meta) acryloyloxypropyl-3'-(TORIPURO pill ammonio) propyl phosphate, 3-(meta) acryloyloxypropyl-4'-(TORIPURO pill ammonio) butyl phosphate, 3-(meta) acryloyloxypropyl-3'-(tributyl ammonio) propyl phosphate, 3-(meta) acryloyloxypropyl-4'-(tributyl ammonio) butyl phosphate, 4-(meth)acryloyloxy butyl-3'-(trimethylammonio) propyl phosphate, 4-(meth)acryloyloxy butyl-4'-(trimethylammonio) butyl phosphate, 4-(meth)acryloyloxy butyl-3'-(triethyl ammonio) propylethyl phosphate, 4-(meth)acryloyloxy butyl-4'-(triethyl ammonio) butyl phosphate, 4-(meth)acryloyloxy butyl-3'-(TORIPURO pill ammonio) propyl phosphate, 4-(meth)acryloyloxy butyl-4'-(TORIPURO pill ammonio) butyl phosphate, 4-(meth)acryloyloxy butyl-3 '- (tributyl ammonio) propyl phosphate and 4-(meth)acryloyloxy butyl -4'-(tributyl ammonio) butyl phosphate etc. is mentioned. Furthermore, the derivative of the monomer of the maleic acid by which 1-2 radicals shown by the general formula 1 were esterified, a fumaric acid, and an itaconic acid etc. can be mentioned.

0016 These kinds thru/or two sorts or more can be mixed and used for the aforementioned monomer. From points, such as availability, the 2-methacryloiloxy-ethyl-2'-(triethyl ammonio) ethyl phosphate (it abbreviates to MPC hereafter) shown by the degree type is mentioned preferably.

0017

Formula 7



0018 The polymer (A) used for this invention is a polymer which consists of a copolymer of the monomer and the monomer which can be copolymerized which has the side chain expressed with said general formula (1) of the above-mentioned publication. As this monomer that can be copolymerized For example, methyl (meta) acrylate, ethyl (meta) acrylate, Propyl (meta) acrylate, butyl (meta) acrylate, pentyl (meta) acrylate, Hexyl (meta) acrylate, heptyl (meta) acrylate, octyl (meta) acrylate, Alkyl (meta) acrylate, such as nonyl (meta) acrylate and DESHIRU (meta)

acrylate, Acrylamide, dimethyl (meta) acrylamide, diethyl (meta) acrylamide, (Meta) Acrylamide (meta) system monomers, such as dipropyl (meta) acrylamide and dibutyl (meta) acrylamide, Vinyl ester system monomers, such as styrene system monomers, such as styrene and methyl styrene, and vinyl acetate, Vinyl ether system monomers, such as ethyl vinyl ether and butyl vinyl ether, Hydrocarbon system monomers, such as ethylene, a propylene, and an isobutylene, dimethyl fumarate, Dibasic acid ester system monomers, such as diethylfumarate, dipropyl fumarate, dibutylfumarate, dipentyl fumarate, dihexyl fumarate, and diheptyl fumarate, etc. can be mentioned. Alkyl (meta) acrylate can be more preferably mentioned among these monomers.

0019 As for the presentation ratio of the monomer which has the side chain expressed with said general formula (1) which constitutes the polymer (A) used for this invention, and the monomer in which the aforementioned copolymerization is possible, it is desirable that it is five mols : 95 mols - 95 mols : five mols, and it is more desirable that it is ten mols : 90 mols - 90 mols : ten mols. Since it will be hard coming to form a particle if **than 95 mol% more it will be hard to discover biocompatibility if there is less monomer which has the side chain expressed with said general formula (1) than five mol%, and** , it is not desirable.

0020 As for the molecular weight of the polymer (A) used for this invention, it is desirable that it is 1,000-1,000,000, and 5,000-500,000 are more desirable. When using especially as a drug carrier, it is desirable to use 5,000-50,000. When molecular weight is smaller than 1,000, since the thing of the molecular weight which exceeds 1,000,000 by the stability of a particle becoming low is difficult to manufacture, it is not desirable.

0021 As a biodegradable polymer (B) used for the macromolecule particle of this invention For example, polyglycolic acid, polylactic acid, a polyglycerin acid, Pori tartronic acid, The copolymer of the Pori malic acid, the Pori tartaric acid, and the above-mentioned polyhydroxy acid, Glycolide-lactin copolymer and Pori p-dioxa non, a glycolide-trimethylene carbonate copolymer, Pori (amide-urethane), Pori (epsilon-amino hexanoic acid), poly urea, A polyanthus hydride, Pori (amide-enamine), polyphosphazene, polyvinyl alcohol, polyvinyl acetate, polyacrylic ester, protein, a cellulose, starch, etc. can be mentioned. A polyhydroxy acid can be mentioned more preferably.

0022 As for the molecular weight of the biodegradable polymer (B) used for this invention, it is desirable that it is 1,000-1,000,000, and especially 5,000-500,000 are desirable. When molecular weight is smaller than 1,000, the stability of a macromolecule particle tends to become low, and when larger than 1,000,000, adjustment of a macromolecule particle is difficult.

0023 The macromolecule particle of this invention can be manufactured by distributing a biodegradable polymer (B) solution in (Polymer A) water solution. The concentration of a polymer (A) has 1 ppm - desirable 100,000 ppm, and 100 ppm - its 10,000 ppm are especially desirable. Adjustment of a particle is difficult if **than 100,000 ppm more actuation will become complicated since concentration is thin if fewer than 1 ppm, and** .

0024 In order to adjust a biodegradable polymer (B) solution, it is desirable to use a solvent, for example, it can mention preferably benzene, toluene, a xylene, a pentane, a hexane, a heptane, an octane, an acetone, a methyl ethyl ketone, a methylene chloride, chloroform, a carbon tetrachloride, ethyl acetate, butyl acetate, dimethylformamide, dimethylacetamide, dimethyl sulfoxide, diethylether, a tetrahydrofuran, water, etc.

0025 The concentration of a biodegradable polymer (B) has 0.001 % of the weight - 50 desirable % of the weight, and 0.01 % of the weight - its 10 % of the weight is desirable. By concentration lower than 0.001 % of the weight, since concentration is thin, actuation becomes complicated, and in concentration higher than 50 % of the weight, adjustment of a particle becomes difficult. The emulsification and the distributed approach which are generally used can be used as an approach of distributing a biodegradable polymer solution (B) in (Polymer A) water solution. Moreover, the solvent used in order to adjust a biodegradable polymer (B) solution can be easily removed using distilling off, dialysis, etc.

0026

Effect of the Invention The macromolecule particle of this invention consists of the polymer (A) and biodegradable polymer (B) which contain the monomer which has the side chain expressed with a general formula (1) as a polymerization component, and since a polymer (A) exists on the surface of a biodegradable polymer (B), it can discover the outstanding biocompatibility resulting from the monomer which has the side chain expressed with a general formula (1). Furthermore, since it is decomposed in in the living body, the biodegradable polymer (B) is excellent in safety. Therefore, the macromolecule particle which has biocompatibility and safety can be offered.

0027

Example Hereafter, an example explains to a detail. In addition, the analysis apparatus and measuring method which were used are as follows.

1. Measurement of the MPC content in a polymer (mol %); measurement of 1 H-MNR to the MPC origin - N(CH3) 3 and butyl of n-butyl methacrylate - It computed from CH3.

2. measurement **of F-potential** ; -- measurement of the F-potential of a particle -- a model; F-potential measurement machine and the product made from the Otsuka electron -- ELS-800 and a migration solvent were performed using the phosphoric-acid physiological saline.
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The measurement 2; electron microscope model of particle size of a particle; it observed, after dyeing and carrying out carbon shadowing of the JEOL make, JSM-5400, and the condition; particle with an osmic acid.
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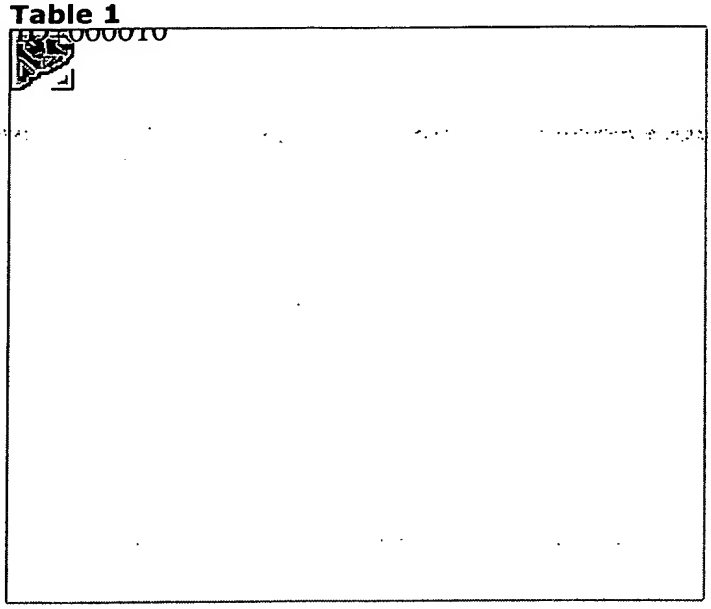
0028 Into synthetic example 1 ethanol, one mol /of azobisisobutyronitrils was further adjusted to the concentration of 5 millimols / liter as a polymerization initiator l., and the polymerization of the monomer constituent (30/70; mol %) of 2-(methacryloyloxy) ethyl-2-(trimethylammonio) ethyl phosphate (Following MPC and brief sketch) and n-butyl methacrylate (Following BMA and brief sketch) was carried out at 60 degrees C for 2 hours. After having dropped the reaction mixture at the ether after reaction termination, carrying out the precipitating copolymer the ** exception and removing a residual monomer, reduced pressure drying was carried out and the MPC-BMA copolymer (it outlines Following PMB) was obtained. The analysis result of obtained PMB was shown below.
yield: -- MPC content **in a 70 % of the weight copolymer** : -- 30 mol %IR(cm-1):2800-3000, 1730 and 1400, and 1200 molecular weight: MW=68,000 **0029** PMB compounded by the example 1 of example 1 composition was dissolved in distilled water, and it adjusted to the concentration of 1 mg/mL. Next, 20mg (PLA-0020, the Wako Pure Chem make, weight average molecular weight = 20,000) of Polly L-lactic acid was dissolved in methylene chloride 2mL. It dropped one drop of methylene chloride solution of the above-mentioned polylactic acid at a time, having soaked the PMB water solution into the ice bath, and stirring by 400rpm. Sonication equipment (product made from BRANSON SONIC POWER COMPAN) performed processing for 30 minutes after dropping termination. After distilling off a methylene chloride under reduced pressure, the particle was made to sediment according to centrifugal separation (for **10300** G or 30 minutes). After having removed the supernatant, adding distilled water 40 mLs and re-distributing a particle, the particle was made to sediment according to centrifugal separation (for **10300** G or 30 minutes). The same actuation was repeated a total of 3 times, and the macromolecule particle was obtained. The obtained macromolecule particle was distributed, vibration frequency was measured using the Xtal dispatch child (Hokuto Denko make), and the concentration of a particle was computed. Moreover, the particle size of the obtained particle was measured using the atomic force microscope and the electron microscope. Furthermore, F-potential measurement of a particle was performed.
yield **of a macromolecule particle** : -- particle-size **of 10% macromolecule particle** : -- about 100nm F-potential: -- as a result of the -10mV above-mentioned measurement, the particle was spherical and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.
0030 Except having changed into 0.5 mg/mL the PMB water-solution concentration used in the example 2 example 1, the same actuation as an example 1 was performed, and the target macromolecule particle was obtained.
yield **of a macromolecule particle** ; -- particle-size **of 10% macromolecule particle** ; -- about 160nm F-potential: -- the particle was spherical as well as the -10mV example 1, and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.
0031 Except having changed into 0.1 mg/mL the PMB water-solution concentration used in the example 3 example 1, the same actuation as an example 1 was performed, and the target macromolecule particle was obtained.
yield **of a macromolecule particle** ; -- particle-size **of 10% macromolecule particle** ; -- about 170nm F-potential: -- the particle was spherical as well as the -10mV example 1, and it became clear that the trimethylammonio ethyl phosphate radical exists in the particle front face.
0032 The giant-molecule particle adjusted to the phosphoric-acid buffer water solution (concentration 0.1 mg/mL) of example of reference 1 cow serum albumin in the example 1 was added, and it incubated at 37 degrees C for 3 hours. The circular dichroism spectrum of cow serum albumin was measured after processing, and the content of the alpha helix in cow serum albumin

was calculated. The result was shown in Table 1.

0033

Table 1



0034 From the above result, not being influenced by the concentration of a macromolecule particle becomes clear and it can be said that it has biocompatibility.